REMARKS

Claims 10-15 are pending in this application. Claims 10-14 have been amended. Support for the language "pins" is found at least at page 9, paragraph [0038]. Support for the term "mist" is found at least at page 4, paragraph [0009] of the specification. Support for the language "diameter ranging from 10 microns to 100 microns" is found at page 9, paragraph [0039] and Example 1 in the specification. Support for the language "without forming a wetting film" is found at least at page 10, paragraph [0040]. Support for the language "wherein said dots are not covalently bound to a substrate" is found at page 4, paragraph [0008]. No new matter has been added. In view of the foregoing amendment and the following remarks, Applicant believes that the asserted rejections should be withdrawn and that all pending claims 10-15 are in condition for allowance.

35 U.S.C. § 112, second paragraph, rejection

Claims 10-15 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner makes the following assertions: that in claim 10, line 2, it is not clear if the "computer software" in line 2 is the same as the "operating software" in line 7; that in claim 10, line 2, it is not clear whether the operating instructions are in the dot applicators of line 3 or the device for aerosol generation in line 4; that in claim 10, line 6, it is not clear whether the xy positioner is in the dot applicators in line 3 or in the device for aerosol generation and whether the xy positioner in claim 10 is the same xy positioner recited in claim 12, line 6; that in claim 10, line 7, it is not clear whether the computer and operating software is in the dot applicators or the device for aerosol generation, stating that if the computer and software reside in only one of the device, then it also is not clear if a computer is being claimed for the other device; that in claim 10, line 8, it is not clear whether the chamber is in the dot applicators or the device for aerosol generation; that in claim 11, lines 1-2, it is not clear whether the system further comprises one or more subcomponents; that in claim 12, line 16, it is not clear whether Applicant intends a gas flow meter and controller or a gas flow meter or controller; that in claim 12, line 6, it is not clear whether Applicant intends an exhaust and filtration fan or an exhaust or filtration fan; and that in claims 13 and 14, "said microsyringes" lack antecedent basis.

Claims 10-14 have been amended to address each of these grounds for rejection, thus obviating this rejection.

35 U.S.C. § 103 Rejections

Claims 10 and 11 stand rejected under 35 U.S.C. § 103(a) as being obvious over Henderson et al. (U.S. Patent No. 6,573,369) in view of Eipel et al. (U.S. Patent No. 6,737,024), and further in view of Church (U.S. Patent No. 6,432,360) and Engle et al. (U.S. Patent No. 6,521,325). Claims 10-14 stand rejected under 35 U.S.C. § 103(a) as being obvious over Henderson et al. in view of Tisone and further in view of Church. Claim 15 stands rejected under 35 U.S.C. § 103(a) as being obvious over Henderson et al. in view of Tisone and Church and further in view of French et al.

Applicant respectfully traverses these rejections and requests that the rejections be reconsidered and withdrawn.

The undersigned representative of the Applicant appreciates the courtesies extended by the Examiner in an in-person interview conducted on May 11, 2006, in which claim amendments were discussed to clarify the claims and to distinguish the claims over the art of record. The Examiner stated that the structural limitations discussed, if added to the claims, would be helpful in distinguishing the claims over the art of record and any amendment(s) and declaration would be considered when formally entered.

The claimed invention is directed to an assay system comprising a computer and a set of operating instructions resident in computer software of the computer for operating, a set of reactant dot applicator pins, a separate device for biological sample aerosol mist generation, an xy positioner operatively connected to the dot applicator pins, and a chamber within the device for biological sample aerosol mist generation for control of biological samples, wherein the dots have a diameter ranging from 10 microns to 100 microns and have one or more constituents therein, wherein the aerosolized biological sample mist droplets are applied simultaneously by the separate device for sample aerosol generation without forming a wetting film, for computer-enhanced assay of any reaction between the sample mist droplets and the constituents, and wherein the dots are not covalently bound to a substrate.

Accompanying this Response is the signed Declaration of Scott L. Diamond. The declarant, Scott L. Diamond, is a citizen of the United States and resides at 610 Yale Rd., Bala Cynwyd, PA 19004, Montgomery County. Dr. Diamond graduated from Cornell University in 1986 with a bachelor's degree in chemical engineering and from Rice University in 1990 with a Ph.D. in chemical engineering. From 1990 to 1997, Dr. Diamond

was a faculty member at the State University of New York. From 1997 to the present, Dr. Diamond has been a faculty member of Penn Engineering, where he holds the Arthur E. Humphrey Chair of Chemical and Biomolecular Engineering and Bioengineering. In addition, Dr. Diamond is the Associate Director and Charter Member of The Institute for Medicine and Engineering; Director, Biotechnology Program; and Director, Penn Center for Molecular Discovery.

Dr. Diamond, as an expert in the field of biotechnology, attests, in Paragraph 5 of the Declaration, that never has it been possible before the present invention and, indeed, is extremely difficult, to rapidly and uniformly deliver an aerosolized mist to adherent droplets, in which each droplet has a diameter ranging between 10 mm and 100 mm and separated only by a center to center distance of only 50 mm to 500 mm, without cross-contaminating the droplets or changing the position of each droplet. Additionally, in Paragraph 6, Dr. Diamond attests that the aerosolized biological sample mist of the claimed invention can be deposited in a highly uniform manner without the generation of a continuous wetting film, which would destroy the positional isolation of each adherent droplet.

According to Dr. Diamond, as stated in Paragraph 7, the claimed invention provides the unexpected finding of the generation of an aerosolized mist that is so fine so as to deposit the aerosolized mist on an array to mix with the adherent droplets while at the same time evaporating very rapidly when the aerosol mist hits the substrate. This is depicted in FIGS. 13A-13D (Exhibit A), which shows that each reaction droplet is and remains isolated from every other reaction droplet, with each reaction droplet thus remaining positionally unperturbed and unmoved, as shown in FIG. 17 (Exhibit B).

The above-described unexpected phenomenon of the claimed invention, namely, of reaction droplet isolation even after application of an aerosolized mist containing a biological sample is shown with striking clarity in FIG. 1.ED (Exhibit C). As explained by Dr. Diamond, in Paragraphs 8-9, FIG. 1.ED contains four panels which show the delivery of the aerosolized mist to each droplet, in which the aerosol evaporates between the droplets within 7 seconds while never reaching a percolation limit, thereby preventing cross-contamination of the droplets. This surprising and unexpected reaction isolation between each droplet is shown clearly in FIG. 2.ED (Exhibit D). This figure shows the aerosol deposition of a mist with a green dye (the paler droplets) on an array containing alternating rows of droplets containing blue dye (the whiter droplets) and rows of droplets lacking dye

(the paler droplets). This unexpected reaction isolation between each droplet is maintained indefinitely, whereby the blue dye does not cross-contaminate into the rows lacking the blue dye.

Furthermore, according to Dr. Diamond, as stated in Paragraph 10, there is an exceedingly novel and unexpected phenomenon of the claimed invention which occurs between the deposited aerosol mist and the adherent droplets, as depicted in FIG. 23 (Exhibit E). This figure shows the occurrence of a zone of clearing due to the unexpected curvilinear trajectories of the deposited aerosol mist in close proximity to the droplets. This cleared zone around each droplet further enhances each droplet's isolation from every other droplet, creating a virtual containment zone without the need for any special hydrophobic or electroactive coating of the planar substrate, and without the need for any physical containment between the droplets, such as well walls. This unexpected phenomenon is shown schematically in FIG. 3.ED (Exhibit F). The dynamics of this unexpected phenomenon is shown in FIG. 4.ED (Exhibit G), where the cleared containment zones are clearly visible without the use of wells or a hydrophobic surface coating.

Dr. Diamond attests, at Paragraph 11, that he is familiar with the cited art of record. In particular, Dr. Diamond understands Henderson et al. to disclose an array comprised of a surface and at least one molecular domain deposited on the surface, in which each domain is 1 micron or less (column 6, line 19 *et seq.*). The deposition device for depositing the molecular domain includes an atomic force microscope (AFM) tip, rather than the applicator pins of the claimed invention. Dr. Diamond attests that nowhere do Henderson et al. disclose or suggest an assay system comprising a computer and a set of operating instructions resident in computer software of the computer for operating, a set of reactant dot applicator pins, a separate device for biological sample aerosol mist generation, an xy positioner operatively connected to the dot applicator pins, and a chamber within the device for biological sample aerosol mist generation for control of biological samples, wherein the dots have a diameter ranging from 10 microns to 100 microns and have one or more constituents therein, wherein the aerosolized biological sample mist droplets are applied simultaneously by the separate device for sample aerosol generation without forming a wetting film, for computer-enhanced assay of any reaction between the sample mist droplets and the constituents, and wherein the dots are not covalently bound to a substrate.

With respect to the disclosures of Eipel et al. and Church, it is clear that neither reference teaches nor discloses an aerosol generation device in which a set of reactant dot applicator pins are capable of creating a plurality of reaction spots and a biological sample mist is applied simultaneously by a separate sample aerosol generation device. Rather, Eipel et al. disclose a punch technique for applying a sample and reagents in liquid, not aerosol misted, form (column 4, lines 32-40) and Church solely discloses inkjet deposition in which small drops of liquid, not an aerosol mist, are applied to a support (column 27, line 22), as corroborated by Dr. Diamond at Paragraph 12.

With respect to Engle et al., this reference is cited solely for the purpose of disclosing the use of a printer that is computer-controlled with a set of operating instructions in the computer software. Engle et al. disclose microembossed transparent ink jet receptor films which are suitable for use with desktop ink jet printers for the production of presentation quality overhead transparencies. Engle et al. briefly mention, in the background section, that components of an inkjet system can be grouped into three categories: computer, software, printer; ink; and receptor medium, in which the computer, software and printer will control the size, number and placement of the ink drops. Nowhere do Engle et al. teach or suggest an assay system comprised of two separate computer-controlled devices in which the first computer-controlled device applies reactant dots onto a microarray and the second computer-controlled device generates and applies simultaneously a biological sample aerosol, as corroborated by Dr. Diamond at Paragraph 14.

With respect to Tisone, this reference discloses only a single reagent dispensing apparatus for dispensing atomized chemical reagents onto a membrane in order to form a diagnostic test strip. Nowhere does Tisone teach or suggest an assay system comprised of a set of reactant dot applicator pins and a separate device for biological sample aerosol mist generation, in which the reactant dot applicator pins deposit reactant dots onto a microarray and the separate device for biological sample aerosol mist generation applies simultaneously a biological sample aerosol mist, as corroborated by Dr. Diamond at Paragraph 15.

With respect to French et al., this reference is cited solely for the purpose of disclosing an aerosol generation device in the form of a nebulizer. French et al. disclose a single apparatus for producing a stream of flowing carrier gas and a stream of small droplets in which the droplets are heated in the carrier gas to produce dry particles that can be

analyzed in a suitable analyzer. Nowhere do French et al. teach or suggest an assay system comprised of two separate computer-controlled devices in which the first computer-controlled device applies reactant dots onto a microarray and the second computer-controlled device generates and applies simultaneously a biological sample aerosol, as corroborated by Dr. Diamond at Paragraph 16.

Based on the foregoing understanding of the cited prior art, Dr. Diamond concludes, at Paragraph 17, that Henderson et al. do not teach or suggest the claimed invention, and that the disclosures contained in the Eipel et al., Church, Engle et al., Tisone or French et al. references do not cure this deficiency.

In view of the foregoing amendments and remarks, it is respectfully submitted that all pending claims 10-15 in the present application comply with the requirements of Section 112 and are distinguishable from the cited prior art. Accordingly, reconsideration and withdrawal of the rejection and an early Notice of Allowance are respectfully requested.

Respectfully submitted,

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